Title

Development of a Disease Activity and Responder Index for Psoriatic Arthritis – Report of the Psoriatic Arthritis Module at OMERACT11

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Abstract

This module reflected work within the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) to develop and validate composite disease activity measures in PsA. At OMERACT 8, a core set of domains to be assessed in randomized controlled trials (RCTs) and longitudinal observational studies (LOS) of psoriatic arthritis (PsA) was agreed upon. At OMERACT 10, five proposed composite responder definitions for PsA were reviewed and discussed including new data from the GRACE (GRAppa Composite Exercise) study. At OMERACT 11, ongoing retrospective analyses of RCT data using the three proposed measures (the CPDAI[Composite Psoriatic Disease Activity Index], PASDAS [Psoriatic ArthritiS Disease Activity Score] and AMDF [Arithmetic Mean of the Desirability Function]) were discussed in detail.

There was agreement that developing composite outcome measures for use in RCTs and LOS in PsA was important. Concerns were expressed regarding development of a single measure that encompassed diverse domains such as joint counts, quality of life and disability measures. It was emphasized that the use of any composite measure should include the ability to differentiate between activity in individual domains, such as enthesitis or psoriasis, such

that the impact of each could be assessed independently. It was also agreed that patients would be systematically involved in further development and refinement of composite measures.

Future work planned includes qualitative work with patients to explore their experience of disease activity and statistical modeling to explore how each of the proposed measures will perform in different disease subgroups.

Key Indexing Terms

psoriatic arthritis, clinical outcome measures, assessment, disease activity

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Short Running Footline

OMERACT psoriatic arthritis module 2012

Introduction:

Psoriatic arthritis (PsA) is a multi-faceted disease with involvement of peripheral joints, skin, nails, entheses, soft tissues of the digits (i.e., dactylitis) and axial skeleton. Outcomes research in PsA has generally lagged behind that in rheumatoid arthritis (RA). The lack of validated outcome measures comprising all domains of disease involvement in PsA remains a particular challenge. Many different outcome measures for each of the separate aspects of the disease are available but most are borrowed from related diseases such as RA, axial spondyloarthritis, (AxSpa), or psoriasis and only some have been validated in PsA. Until recently there were no composite outcome measures for PsA that included all of the mentioned aspects of disease involvement.

Composite measures used in RA to assess disease severity and employed in responder indices, such as the Disease Activity Score (DAS) with the related European League Against Rheumatism (EULAR) Response Criteria, or the American College of Rheumatology (ACR) Response Criteria, primarily focus on the assessment of peripheral joint activity. The DAS includes an acute phase response marker and ACR response criteria include acute phase response, pain, and physical function in addition to specific measures of peripheral arthritis but these do not fully represent all aspects of PsA. While used in many RCTs to assess peripheral joint disease activity and indirectly, through the patient global assessment, other aspects of PsA, these composite measures omit direct evaluation of the additional domains of PsA such as enthesitis, dactylitis, axial and skin disease.

Recognition of this dearth of validated outcome measures in PsA led to the formation of a joint Outcome Measures in Rheumatology (OMERACT)/Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) working group to develop a

research agenda of outcome measurement in randomized controlled trials (RCTs) in PsA. There are currently more than 400 members of GRAPPA internationally, including rheumatologists, dermatologists, radiologists, epidemiologists, industry and patient service league representatives.

The first step was an outcome measures workshop in PsA held at OMERACT 7 (Asilomar, USA, 2004). Discussion on potential domains for inclusion in RCTs in PsA led to a research agenda to identify optimal measures for each aspect of psoriatic disease and to develop effective instruments where none existed (1). Significant further progress was made at the OMERACT 8 conference (Malta, 2006) . There, consensus was reached on the core domain set for PsA trials(2), based on a series of projects conducted following OMERACT 7 including: a clinician Delphi exercise and data mining from completed RCTs. At OMERACT 8, no data were available on composite measures designed to assess multiple domains of PsA.

Since OMERACT 8, GRAPPA has been actively working to develop reliable diagnostic and assessment tools for PsA, including clinical, laboratory, imaging, tissue analysis, and composite measures of disease activity. This work is pursued both in individual clinical research centers as well as collaboratively amongst members of the group. At the GRAPPA Annual Meeting in 2008 (Leeds, UK) data from application of previously, work on different proposed composite indices were presented, including many of the measures discussed below. Different potential approaches were also discussed, e.g., the development of the DAS in RA and the Ankylosing Spondylitis Disease Activity Score (ASDAS) as well as the British Isles Lupus Assessment Group (BILAG) score in systemic lupus erythematosus(4). Breakout groups discussed these different options and a large collaborative exercise (GRACE) was

proposed to initiate the development and validation of a GRAPPA/OMERACT composite disease activity measure for PsA(5). This work led to a special interest group (SIG) at OMERACT 10 being convened in 2010. At this session results of ongoing work with the GRACE dataset and analysis of some proposed composite measures was presented.

Proceedings during the Module

At OMERACT 11 a literature review of measures used in PsA was presented to summarise existing individual measures designed to assess varying aspects of disease. An individual with PsA spoke about her experiences of developing PsA and the myriad ways her disease has affected her, highlighting the importance of measuring domains other than just articular or skin disease. Oliver FitzGerald presented a summary of the evidence supporting use of the Composite Psoriasis Disease Activity Index (CPDAI) including a recent analysis from the Psoriasis Randomised Etanercept Study in Subjects with Psoriatic Arthritis (PRESTA) data. Philip Helliwell presented the methodology for development of the Psoriatic Arthritis Disease Activity Score (PASDAS), a weighted composite measure analogous to the DAS in RA, and for the Arithmetic Mean of the Desirability Function (AMDF), a non-weighted score where all variables are transformed to the same scale and combined arithmetically. Finally discussion with participants at OMERACT was designed to highlight issues and methodologic points regarding development of the composite measures proposed to date.

Background and Aims of the module

Philip Mease provided a brief summary of the domains considered important in RCTs in PsA, as decided at OMERACT 8. He highlighted different types of composite outcome measures in terms of design, and summarized the argument for a comprehensive composite index in

PsA. He briefly reviewed work and introduced the aims of the module at OMERACT 11, namely:

1. Present a literature review of various outcome measures that individually reflect different domains of PsA, and compare them with other composite measures of disease activity in RA as well

2. Highlight the patient's perspective with an illustration of the many ways in which this disease can affect a single patient over time.

3. Present work to date assessing performance of the proposed PsA responder indices in datasets from completed RCTs and independent populations.

4. Provide a forum for discussion of these proposals and an opportunity for feedback and debate.

5. Define issues which remain in the research agenda regarding domains and instruments for their assessment in PsA.

Review of outcome measures used in PsA clinical trials

A number of outcome measures have been developed and used in PsA to measure different aspects of the disease (2, 6-11) (Table 1).

For arthritis, the majority of measures used in RCTs in PsA were adopted from RA. Dr Laura Coates summarized data regarding the use of ACR and DAS outcomes in PsA, explaining that these measures had been shown demonstrated responsive in polyarticular PsA as evident from differing clinical trial datasets (3). Deficiencies included that 28-joint counts are not reliable in PsA and there are no data concerning the validity of these measures in oligoarthritis. The Psoriatic Arthritis Response Criteria (PsARC) was the first composite measure designed specifically for PsA in an RCT of sulfasalazine in PsA by Clegg, et al. and utilizes a composite measure of tender and swollen joint counts with patient and physician

global assessments of disease activity(12). However, it was empirically derived and does not specifically incorporate other features of PsA such as enthesitis, dactylitis, or axial or skin disease. The use of the physician and patient global visual analogue scale (VAS) scores may partially reflect activity in these elements of disease depending on the wording of the VAS questions.

A brief summary of new articular composite measures specifically designed for PsA was presented, i.e., the PsA Joint Activity Index (PsAJAI) and the Disease Activity in PSoriatic Arthritis (DAPSA). Both scores have specifically excluded skin disease activity, although for different reasons. The PsAJAI,a response measure using a 30% reduction in disease activity as the cut-off, was developed from and tested in two independent samples from RCT datasets of tumor necrosis factor (TNF) inhibitors utilizing statistical modeling. Therefore, it has been validated in a predominantly polyarticular, not oligoarticular, subset of disease. It ultimately excluded a measure of skin disease activity because the magnitude of skin disease improvement in these trials was so large that it overwhelmed responses in articular disease(13). The DAPSA score(14) was suggested for PsA after principal component analysis of data in 105 PsA patients found that the key disease domains were represented by measures included in the DAREA (Disease Activity index for Reactive Arthritis), originally developed for reactive arthritis(15). In this analysis, skin disease activity was proposed as a component but did not quite reach significance, possibly due to the low level of skin disease in this specific patient cohort. Components of the DAREA include swollen and tender joint counts, patient global score, pain score and C-reactive protein (CRP). Ultimately, both the PsAJAI and the DAPSA have included only specific measures of articular disease although the global patient reported scores for disease activity and pain may partially encompass other elements of PsA but it unclear to what extent.

To measure psoriasis, several skin measures have been developed for use in psoriasis RCTs and LOS. Interestingly, patients enrolled in PsA clinical trials often have low body surface area (BSA) involvement of psoriasis and thus may not be reliably evaluated with the Psoriasis Area and Severity Index (PASI) score(16). The PASI exhibits poorer performance in subjects with less than 3% BSA involvement. A "target lesion" score may be used, where one lesion is evaluated over the course of the study(6), but this does not reflect the total extent of disease involvement nor which areas are involved. Newer scoring methods such as the lattice system Physician's Global Assessment of psoriasis (PGA)(17) and the Copenhagen Psoriasis Severity Index(18) were also briefly discussed. Nail involvement is also a common problem in psoriasis and particularly in PsA. The Psoriasis Nail Severity Score (PNSS), developed in Bath(19) has been utilized in studies and even more recently, several PsA trials have successfully incorporated a modified Nail Psoriasis Severity Index (mNAPSI) score for evaluation of responses in nail involvement(20).

Recognizing the importance of enthesitis and dactylitis as domains, measures for these clinical features have evolved over the past several years and are now routinely performed. Several measures of enthesitis, which assess different groups of entheseal insertion sites, are being utilized and it is anticipated that as these are evaluated, a single measure may emerge as standard for PsA. Measures specifically developed for PsA such as the Leeds Enthesitis Index (LEI) and developed in a mixed group of spondyloarthritis (SpA) patients, such as the SPARCC (Spondyloarthritis Research Consortium of Canada) enthesitis index are now being used in ongoing research. These have identified different entheseal points that may be more important in PsA in comparison with older measures such as the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES). As part of the GRACE dataset, all clinical entheseal points in any of the accepted enthesitis indices are evaluated which is allowing assessment of

how the different measures compare in a heterogenous real-world cohort and whether a new measure with a greater validity can be developed. It was highlighted that up to half of patients with PsA experience dactylitis as some point in their disease course. Measurement of this phenomenon has been evaluated by Helliwell et al who have compared existing measures such as digit counts and semi-quantitative scoring of dactylitis and have developed the dactylometer which allows quantification of clinical digit swelling(21, 22).

Spinal involvement in PsA has generally been under-researched with no specific clinical trials in this group of patients. Spinal involvement is not commonly measured in RCTs in PsA, partly due to difficulties assessing this disease component. Physical examination measures of the spine are reliable in axial PsA(23) and reflect not only disease activity but also significant cumulative damage. Measures of axial disease activity used in AxSpa, including the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and ASDAS have been shown to correlate with constructs of disease activity in axial PsA(24-26), but not to differentiate between peripheral and axial disease activity casting doubt on their construct validity in PsA.

A patient's perspective

Next, a patient representative provided valuable perspective as an individual with PsA, but also as a physician who treats PsA and conducts research in PsA. Highlights of the presentation included discussion about the initial symptoms which were primarily axial and entheseal and although she visited a rheumatologist early in her disease course, she came away without a diagnosis as no significant arthritis or skin disease was present at onset and initial laboratory assessments and radiographs were negative. However, she understood as a rheumatologist what her symptoms meant before her treating rheumatologist did -- ..

Cognizant of the United States' health care system issues around pre-existing conditions and to avoid negative repercussions on her ability to provide for her family, obtain life insurance for her family as she was the primary breadwinner, she didn't return for diagnosis or treatment when synovitis developed about 1 to 2 months later. Instead, she reported she chose to self-manage the disease with minocycline and ibuprofen. She originally thought she had AS, but once she developed onycholysis of her large toenails developed about 6 months into her symptoms, she recognized she most likely had PsA. She shared that the axial symptoms and fatigue had been some of the her worst symptoms, and that she also changed jobs to minimize the impact of stress, travel, and lack of sleep on her health. She recognized in herself complaints that her patients had made to her about, e.g., walking on marbles related to metatarsal pain, hobbling to the bathroom in the morning due to stiffness, keeping nail polish on her toenails to avoid showing evidence of her onycholysis. She appreciated the ability to better comprehend her patients' complaints though suffering from them herself. She also recognized several issues specific to her that her patients had never mentioned: e.g., severe tailbone pain so severe that it made it difficult to sit for more than 30 minutes; or neck pain that made her consider where she sat in a room so she wouldn't have to look up at the stage, turn her head or look up, spend a small fortune on different types of neck pillows, or carry her stethoscope over her shoulder instead of around her neck. Eventually, she returned to her rheumatologist who recognized her reluctance to start a TNF inhibitor, and he prescribed sulfasalazine. She was thrilled as was her rheumatologist when she reported how well sulfasalazine had worked for her symptoms, especially the stiffness and peripheral joint disease. She mentioned that stress and lack of sleep continued to precipitate flares, and she has made it a priority to manage these. She recognized that sulfasalazine has probably been a temporizing measure as it has not worked as well for her axial symptoms or nail disease as it has for her peripheral disease. Her disease and its impact on her and her family life were

evolving and her therapy and disease would evolve with her. Ultimately, she stressed that as a researcher and physician as well as a patient, the currently available tools available did not accurately assess the impact of PsA on her disease or her life.

Current proposed composite outcome measures – the CPDAI

Work developing two key composite measures has been initiated and led by members of GRAPPA. FitzGerald and colleagues developed a composite outcome measure based on the GRAPPA treatment grid published by Ritchlin, et al(27). For the CPDAI, a score of 0-3 is assigned to each of the five domains (arthritis, enthesitis, dactylitis, skin and spinal disease) of PsA based on disease activity and impact of disease for this domain (Table 2). The scores are added together to give a total score of 0-15, thus providing an overall assessment of disease activity(28). One concern raised during the development of this measure was that patients with severe disease activity in only one domain may be disadvantaged by a relatively low total score. Two potential solutions have been proposed: first that anyone with a single domain scored as severe would be classified as "severe" overall; second a "modified CPDAI", where the total score is divided by the number of active domains involved yielding a mean score.

Oliver FitzGerald presented validation data for CPDAI from analysis of the PRESTA data. Because PRESTA was an RCT comparing two doses of etanercept (50mg each week and 50mg twice weekly) in a large number of patients with both active psoriasis and PsA(29), it provides an ideal dataset with which to assess the sensitivity of composite disease activity measures. Supporting evidence was that individual measures of joint disease, enthesitis and dactylitis showed similar changes between higher and lower doses of etanercept, but a superior response was evident with the higher dose for skin disease. There were a few

limitations of this dataset. Like many RCTs of PsA, the majority of patients had polyarticular disease despite not being an inclusion criterion, so this dataset does not provide evidence for responsiveness of these measures in oligoarthritis. Like many RCTs in PsA, there was no specific assessment or measure of axial disease in this trial. For this reason, a modified CPDAI assessing four domains (peripheral joint disease, skin, dactylitis and enthesitis) was scored from 0-12 rather than 0-15.

The CPDAI showed good responsiveness to change and identified a significant difference between treatment groups at 12 weeks that was likely driven by the differential response in skin disease ($p=0.049$). In stepwise regression analysis, enthesitis, the Health Assessment Questionnaire (HAQ), dactylitis and the Dermatology Life Quality Index (DLQI) all contributed significantly to the CPDAI values at baseline(30). In comparison, the DAPSA score showed a significant improvement between baseline and 12 weeks in both treatment groups but did not identify a significant difference between the treatment groups at week 12. Thus, while both the DAPSA and CPDAI show responsiveness in measures of arthritis, the CPDAI has a potential advantage in that it can also reflect changes in the other domains of PsA.

GRACE

Following the GRAPPA annual meeting in 2008 and as part of the preparation for OMERACT 10, GRAPPA initiated GRACE which aimed to develop an inclusive composite outcome measure based on real patient data. Longitudinal observational data were collected on a large cohort of PsA patients internationally. Individual outcomes assessing disease activity in all of the domains of PsA, as well as patient reported outcome measures are being collected. Where no consensus had been reached regarding optimal outcome measures for

each component of disease, e.g. enthesitis, multiple measures were collected to allow comparison of different indices. Patients were classified by their treating physician into two groups: those with active disease requiring a treatment change and patients who in the opinion of their treating physician have low disease activity or are in remission. The two groups were then be compared to see where significant differences exist between them and which individual outcome measures account for this difference.

Recruitment to GRACE completed with baseline data on 503 patients with PsA collected and follow up data also available. Analysis of the many outcome measures included in the dataset has shown a difference in all key variables encompassing arthritis, skin disease, enthesitis, dactylitis, axial disease, functional ability and quality of life for those undergoing treatment change and those not, except for the mNAPSI, Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), erythrocyte sedimentation rate (ESR) and Bath Ankylosing Spondylitis Metrology Index (BASMI).

Current proposed composite outcome measures – the PASDAS

The first methodology pursued by the OMERACT PsA group was to develop a weighted composite disease activity score called the PASDAS utilizing methodology used to develop the DAS and ASDAS. A principal component analysis was performed for all variables included in disease activity measures with transformation for all variables to improve variable distribution. Factor analysis identified five components which were (1) patient and physician VAS scores of disease activity, (2) skin activity, (3) tender joint count and enthesitis, (4) swollen joint count and dactylitis, and (5) CRP. However with regression analysis, nearly 80% of variability (adjusted R2) was provided by the patient global disease visual analog scale (VAS) and over 90% by just three VAS scores (patient global assessment, patient

assessment of skin disease, and physician global assessment) using the Cauli standardized VAS questions for PsA(31). At OMERACT 10 and at a later GRAPPA meeting adjacent to EULAR 2010, Philip Helliwell therefore proposed the Psoriatic Arthritis Disease Activity Score (PASDAS) as a composite of three VAS scores. Significant concern was voiced about using just three subjective VAS scores to measure disease activity, particularly by GRAPPA attendees from sponsors who felt that such a disease activity measure would not be supported by regulatory authorities as a robust tool.

Following this discussion, a revised PASDAS was developed. Principal component analysis revealed 7 components which approximated to the following domains: patient reported measures (excluding the mental component summary score [MCS] of the Medical Outcomes Survey Short form-36 [SF-36]), skin, peripheral joint counts, dactylitis, enthesitis, acute phase response and the SF-36 (MCS). In the subsequent forward stepwise regression (FSR), two of the variables (patient and physician global VAS scores) accounted for approximately 90% of the total variance in scores (as seen in the previous incarnation of the PASDAS). A hierarchical multiple regression analysis then considered these variables where both global VAS scores were entered in step 1, dactylitis, enthesitis, CRP, swollen joint count and SF-36-PCS (the physical component summary score of the SF-36) in step 2, and finally tender joint count and SF-36 MCS (neither of which were significant in the FSR) in step 3. The SF-36 MCS did not contribute to the model variance and was therefore omitted from the final PASDAS(32).

The final PASDAS is represented by the following equation:

PASDAS = (((0.18 x √Physician global VAS) + (0.159 x √Patient global VAS) - (0.253 x √SF36 - PCS) + (0.101 x LN (Swollen joint count + 1)) + (0.048 x LN (Tender joint count +

1)) + (0.23 x LN (Leeds Enthesitis Index + 1)) + (0.377 LN (tender Dactylitis count + 1)) + (0.102 x LN (CRPmg/dL + 1)) +2)*1.5.

Current proposed composite outcome measures – the AMDF

The second approach was that suggested by Fransen et al(33), where desirability functions were developed for variables deemed important in assessing disease activity, based on core domains selected for PsA RCTs at OMERACT 8(2). The desirability function can be used to combine multiple responses into one measure by translating each variable onto the same scale from 0 (a completely unacceptable or undesirable level) to 1 (a completely desirable or ideal response value). Then these transformed variables can be averaged to give a total score. Desirability functions for tender and swollen joint counts, HAQ and the patient global assessment of disease activity VAS were derived using expert consensus data gathered by an internet based survey of GRAPPA members during development of the minimal disease activity score(34). Remaining functions (patient VAS for skin, patient VAS for joints, PASI, and Psoriatic Arthritis Quality of Life index (PsAQoL) were developed with expert consensus data obtained from 109 responses in a subsequent internet survey (85 rheumatologists and 24 dermatologists). Cut-offs were determined according to the median of responses (Table 2), and used to transform each variable into linear functions ranging from 0 (totally unacceptable state) to 1 (normal). The 8 transformed variables were then combined using the arithmetic mean (AMDF: arithmetic mean of desirability functions).

Performance of the PASDAS and AMDF in RCT and Observational Cohort Datasets

The OMERACT PsA group aimed to work with many different organizations to apply and test these proposed composite measures in existing RCT and observational cohort datasets prior to the OMERACT 11 module. Unfortunately, many existing datasets do not include all

the variables required to calculate the proposed composite measures. There were also delays in obtaining RCT data for this purpose : only PRESTA data as discussed above were available. A few unavailable variables, e.g., SF-36, PsAQoL, axial disease measures, resulted in minor modifications to calculations of the CPDAI, PASDAS and AMDF composite measures.

All of the composite measures (DAPSA, CPDAI, PASDAS and AMDF) were compared using ANCOVA to compare effect sizes and DAS28 was included as a control measure. The largest effect size was seen with the AMDF score (>2) with a significant difference between effect sizes in the two treatment regimens at 12 weeks. Effect sizes for the CPDAI and PASDAS were also high (~1.5) with lower effect sizes seen with DAPSA and DAS28.

Case Examples

Case 1

A 34 year old man who presented to rheumatology with a six year history of inflammatory back pain. He had had skin psoriasis since childhood and also had active enthesitis affecting one Achilles tendon and both medial femoral condyles and lateral elbow epicondyles. He did not have any peripheral arthritis or dactylitis. He had been treated via his physician with physiotherapy and oral nonsteroidal anti-inflammatory drugs (NSAIDs) with no relief of symptoms.

The elements of all of these scores are shown in table 2. Using the CPDAI, this man scored as follows: Peripheral arthritis – 0, Skin disease – 2, Enthesitis – 2, Dactylitis – 0, Axial disease – 3. His total CPDAI score was 7 indicating severe disease and he was started on a TNF inhibitor due to his severe spinal disease. When applying the PASDAS weighted score

in this case, the total score was 6.03 indicating high disease activity under proposed cut-offs. Using the AMDF score, the total score was 0.53 (scale 0 to 1, 1 is no disease activity) indicating moderate disease activity according to cut-offs defined by Fransen et al (33). The elements of all of these scores are shown in table 2. Interestingly the absence of activity in one element of disease (peripheral arthritis) in this case causes a "perfect" score of 1 to be attributed to both tender and swollen joint counts in the AMDF which inflates the score reducing disease activity from high to moderate using this scoring method

Case 2

This 34 year old lady developed psoriasis at the age of 16 and was then diagnosed with PsA age 22. At the time of this assessment, she was reviewed in a combined clinic and the plan was for her to start a TNF inhibitor. She had active peripheral polyarthritis with dactylitis in 4 toes. She also had axial disease and active skin psoriasis with scattered plaques all over her body. Using the CPDAI, this woman scored a total of 10 indicative of severe disease: Peripheral arthritis – 3, Skin disease – 2, Enthesitis – 0, Dactylitis – 3, Axial disease – 2. When applying the PASDAS weighted score, the total score was 6.78 indicating high disease activity under proposed cut-offs. Using the AMDF score, the total score was 0.46 which indicates moderate disease activity (33). She was started on adalimumab due to her severe disease affecting both the peripheral and axial skeleton. The elements of all her scores are shown in table 3. In this case, the absence of significant skin disease and a relatively low HAQ score decreased the AMDF score to be moderate rather than high as it was for the CPDAI and PASDAS, despite high disease activity in the joints.

Case 3

This 37 year old man had psoriasis since age 4 and then developed PsA at the age of 22. He was also being assessed for anti-TNF therapy. He had oligoarthritis affecting the left 1st metacarpophalangeal (MCP) joint and the right metatarsus. He also had two enthesitis points and dactylitis of the left 4th toe. Given the different aspects of disease and his ongoing active disease, he was started on disease modifying anti-rheumatic drug (DMARD) therapy to control his arthritis and dactylitis. The elements of all of this man's scores are shown in table 4. Using the CPDAI, this man had a total score of 3 indicative of mild disease: Peripheral arthritis – 1, Skin disease – 0, Enthesitis – 1, Dactylitis – 1, Axial disease – 0. When applying the PASDAS weighted score in this case, the total score was 3.74 indicating moderate disease activity, while the AMDF indicated low disease activity with a score of 0.86.

Discussion at OMERACT 11

At the start of the module, participants were asked to vote on two questions. Firstly, they were asked "Are existing measures of composite disease activity developed for rheumatoid arthritis appropriate to measure disease activity/response in psoriatic arthritis?". Secondly they were asked "Do you think a composite measure that only measures inflammatory joint disease and not other musculoskeletal manifestions, nor the skin, is sufficient to measure disease activity in psoriatic arthritis?". For both of these questions, the majority of participants (88% and 93% respectively) voted no. This provided clear support for the concept of a new composite disease activity measure for PsA as agreed upon at OMERACT 10. Some clinicians raised a concern with the concept of a composite score combining very different elements of one disease into a single score, and these may not respond similarly to a single therapy. Disease activity in different domains of PsA may be unrelated, for example

arthritis may flare when skin psoriasis is controlled or vice versa, and there are obviously different treatment implications depending on what element of the disease is active.

However the potential benefit of such a composite score was also highlighted, particularly relevant to assessment of disease severity related to "qualifying" for certain treatment options. Some patients may have moderate disease activity that by involving many different aspects of PsA may severely impact function and quality of life. A composite score that accounts for all domains of psoriatic disease may better reflect such a patient's disease burden. It was agreed that a composite measure was an important research agenda for PsA, but it should be possible to identify the contributions of the individual domains to the total disease activity. This could then guide clinicians in which therapy to choose.

The advantage of all of these proposed composite measures is that they provide a numerical measure of disease activity state that can then be used to assess disease activity at one time point and can also be translated into response criteria defined by a minimum change in the score. Potentially cut-offs for different levels of disease activity can also be defined and used to guide treatment decisions, acting as a target for treatment or a threshold for biologic therapies.

A specific concern was raised regarding the methodology of the PASDAS. In the PASDAS, a measure of quality of life was included besides more specific disease activity measures. This is in contrast to the DAS and ASDAS, similarly developed measures, which do not include quality of life domains and which only have one concept (peripheral joint disease or spinal disease respectively) assessed within each score, although inclusion of such data have been

previously proposed in RCTs in SLE. It was questioned whether this methodology could then be used to develop the PASDAS if such different concepts were being combined.

In terms of future planning, it was discussed that the PsA OMERACT group had exercises proposed to engage with patient research partners for further development of these composite measures and also in qualitative research to ensure that their views of disease activity and assessment are included.

Finally the feasibility of such a composite score, particularly in routine clinical care, was discussed. There are two key feasibility issues with the proposed composite measures. The first is a potential problem for the PASDAS and AMDF related to the complexity of calculating the scores once all of the assessments have been done. Both of these require statistical transformations of all of the variables with complex equations. However all of this could be done using a simple spreadsheet or calculator such as those used for the RA DAS.. The larger feasibility problem affecting all of these proposed scoring systems is the necessity to perform a number of different articular and non-articular outcome assessments to allow calculation of the scores. This has implications on training of rheumatologists and dermatologists to perform these assessments and significant time implications initially if such a scoring system were to be introduced to clinical practice.

At the end of the module and at the final plenary of the OMERACT meeting, a consensus voting exercise was held with all participants to gain agreement on future directions of the PsA OMERACT group. The first two questions related to skin disease assessment. When asked “Given that the skin is such an important component of psoriatic arthritis, should this domain be part of a composite index?” the majority (77%) of participants agreed that skin

disease should be included. They were then asked "Is it sufficient to assume that the patient and physician will take into account the skin component when determining the global disease assessment?". There was a lower agreement to this question, but 62% of patients felt that this could not be assumed. As discussed above, there was concern about feasibility relating to composite indices, with 67% of participants feeling that it was "feasible to assess all clinical domains in a composite disease activity and responder index for psoriatic disease". The final questions related to the three proposed composite indices presented. There was agreement (PASDAS – 78%, AMDF – 67%, CPDAI – 77%) that the further exploration and validation of all of these composite measures was appropriate to continue to investigate. None of them however were at the stage of being proposed for adoption. Further validation within existing datasets is planned as well as exercises with patients.

Conclusion

This module provided a valuable opportunity to present and discuss work on potential composite measures in PsA in a forum for discussion. Three have been proposed but further validation and comparison in other datasets, such as those from existing and future interventional studies, is required.

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Table 1 – Summary of current composite measures

	DAS28	PsAJAI	DAPSA	CPDAI	PASDAS	AMDF
Arthritis (joint counts)	28	66/68	66/68	66/68	66/68	66/68
Skin disease	N	N	N	Y	N	N
Enthesitis	N	N	N	Y	Y	N
Dactylitis	N	N	N	Y	Y	N
Spinal Disease	N	N	N	Y	N	N
Health related quality of life	N	N	N	Y	Y	Y
Physical function	N	Y	N	Y	N	Y
Patient's arthritis disease activity assessment	N	N	N	N	N	Y
Patient's skin disease activity assessment	N	N	N	N	N	Y
Patient's global disease activity assessment	Y	Y	Y	N	Y	Y
Patient's pain assessment	N	Y	Y	N	N	N
Physician's global disease activity assessment	N	Y	N	N	Y	N
Acute phase response	Y	Y	Y	N	Y	N

Table 2 – Example Case 1

Element	Score	CPDAI score	PASDAS score	AMDF score
TJC	0	0	0	1
SJC	0		0	1
HAQ	0.4	2	-	0.84
LEI	5		0.41	-
Dactylitis	0	0	0	-
PASI	8	2	-	-
DLQI	13		-	-
BASDAI	5.6	3	-	-
ASQoL	14		-	-
PsAQoL	9	-	-	0.52
SF36-PCS	30	-	1.39	0.27
VAS patient global activity	65	-	1.28	0.28
VAS patient skin disease activity	10	-	-	0.8
VAS patient joint disease activity	35	-	-	0.58
VAS physician global activity	60	-	1.39	-
CRP	25	-	0.33	-

TJC – tender joint count, SJC – swollen joint count, HAQ – health assessment questionnaire, LEI – Leeds enthesitis index, PASI – psoriasis area and severity index, DLQI – dermatology life quality index, BASDAI – Bath ankylosing spondylitis disease activity index, ASQoL – ankylosing spondylitis quality of life, PsAQoL – PsA quality of life, SF36-PCS – physical component score of short form 36, VAS – visual analogue scale, CRP – C-reactive protein

Table 3 – Example Case 2

Element	Score	CPDAI score	PASDAS score	AMDF score
TJC	13	3	0.13	0.37
SJC	11		0.12	0.36
HAQ	0.88	0	-	0.67
LEI	0		0	-
Dactylitis	4	3	0.60	-
PASI	2.3	2	-	0.82
DLQI	12		-	-
BASDAI	2.16	2	-	-
ASQoL	15		-	-
PsAQoL	17	-	-	0.14
SF36-PCS	30.06	-	1.39	-
VAS patient global activity	65	-	1.28	0.28
VAS patient skin disease activity	10	-	-	0.8
VAS patient joint disease activity	65	-	-	0.28
VAS physician global activity	65	-	1.45	0.28
CRP	24.7	-	0.33	-

TJC – tender joint count, SJC – swollen joint count, HAQ – health assessment questionnaire, LEI – Leeds enthesitis index, PASI – psoriasis area and severity index, DLQI – dermatology life quality index, BASDAI – Bath ankylosing spondylitis disease activity index, ASQoL – ankylosing spondylitis quality of life, PsAQoL – PsA quality of life, SF36-PCS – physical component score of short form 36, VAS – visual analogue scale, CRP – C-reactive protein

Table 4 – Example Case 3

Element	Score	CPDAI score	PASDAS score	AMDF score
TJC	2	1	0.05	0.8
SJC	2		0.11	0.72
HAQ	0.25	1	-	0.9
LEI	2		0.25	-
Dactylitis	2	1	0.41	-
PASI	0	0	-	1
DLQI	0		-	-
BASDAI	0.64	0	-	-
ASQoL	0		-	-
PsAQoL	1	-	-	0.93
SF36-PCS	46.84	-	1.73	-
VAS patient global activity	15	-	0.62	0.86
VAS patient skin disease activity	0	-	-	1
VAS patient joint disease activity	16	-	-	0.75
VAS physician global activity	7	-	0.48	0.8
CRP	18	-	0.30	-

TJC – tender joint count, SJC – swollen joint count, HAQ – health assessment questionnaire, LEI – Leeds enthesitis index, PASI – psoriasis area and severity index, DLQI – dermatology life quality index, BASDAI – Bath ankylosing spondylitis disease activity index, ASQoL – ankylosing spondylitis quality of life, PsAQoL – PsA quality of life, SF36-PCS – physical component score of short form 36, VAS – visual analogue scale, CRP – C-reactive protein